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Pneumonectomy for drug resistant *Myobacterium malmoense*

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Mycobacterium malmoense was first described in 1977[1] and subsequently 11 instances of clinical infection have been reported.[2] Clinical details of the cases are scanty and in none so far as we know was there surgical intervention. We wish to report the first case of *M malmoense* infection where pneumonectomy was life saving, as antituberculous treatment was ineffective.

Case report

A 67 year old housewife was admitted to hospital in January 1981 with a two month history of weight loss (4 kg) and productive cough. She was known to have long-standing bronchiectasis of the left lung. Physical examination showed mediastinal and tracheal deviation to the left, with considerably reduced air entry and coarse inspiratory crackles throughout the left side. A chest radiograph showed new apical shadowing in the left lung, which was fibrotic and contracted owing to the bronchiectasis (fig 1). The haemoglobin concentration was 10·9 g/dl, white cell count (WCC) $9{\cdot}2\times10^9$/l (77% neutrophils), and erythrocyte sedimentation rate (ESR) 70 mm in one hour. Sputum was positive for acid fast bacilli on direct smear but urine was negative. A mycobacterial infection was diagnosed and treatment was started with ethambutol, rifampicin, and isoniazid.

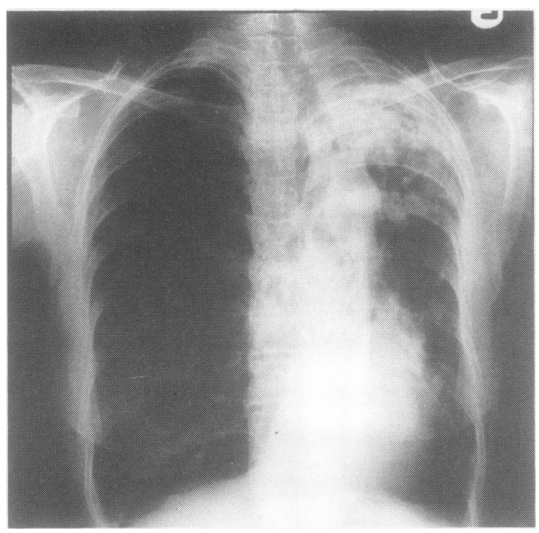

Fig 1 *Chest radiograph in January 1981 showing contraction and fibrosis of the left lung due to bronchiectasis with recent apical shadowing.*

Despite nine months of treatment, the patient failed to improve clinically and continued to lose weight (8 kg between January and December 1981). The sputum remained positive for acid fast bacilli on direct smear and the chest radiograph showed progression of the apical shadowing to the left midzone. The patient was readmitted to hospital in December 1981. Mycobacteria were isolated from sputum obtained in January and December 1981. Both strains were identified as *Mycobacterium malmoense* by the mycobacterium reference unit in Cardiff. The strains were sensitive to ethambutamol, capreomycin, ethionamide, and cycloserine; showed borderline resistance to streptomycin and rifampicin; and were resistant to isoniazid, para-aminosalicylic acid, and thiacetazone. The haemoglobin was 8·6 g/dl, WCC $11{\cdot}6\times10^9$/l (79% neutrophils), and ESR 103 mm in one hour. The temperature chart showed daily spikes to 39·5°C.

After discussion with the mycobacterium reference unit, treatment was started with streptomycin, ethambutol, and ethionamide, as these were effective in vitro. Over the ensuing four weeks the patient continued to deteriorate. Her temperature remained high, her weight loss continued, and her sputum remained positive for acid fast bacilli. As the patient's condition was critical a pneumonectomy was advised as this offered the only hope of survival. After pneumonectomy on 2 January 1982 she made a slow recovery. Her haemoglobin concentration remained stable at 12·7 g/dl after preoperative transfusion and her temperature was normal by 21 January. Sputum specimens obtained in the immediate postoperative period were negative for acid fast bacilli both on direct smear and on culture.

The subsequent advice from the reference unit was to revert to standard antituberculous treatment—that is, rifampicin, isoniazid, and ethambutol. This view was based on the findings of Hunter *et al*,[3] who showed that patients infected with organisms of the *avium-intracellulare* group responded satisfactorily despite in vitro resistance.

The patient was discharged from hospital in March 1982. She was reviewed in June and was found to be well. Her weight had increased by 2 kg, the haemoglobin remained normal, and the ESR was 41 mm in one hour. She had expectorated no sputum since her discharge but laryngeal swabs were negative for acid fast bacilli both on direct smear

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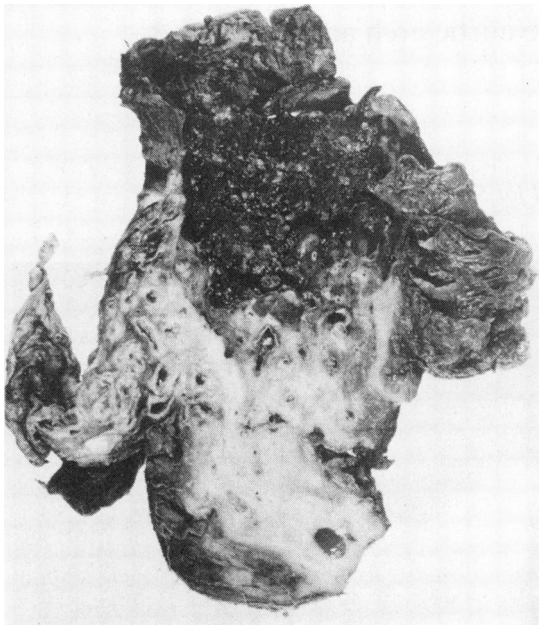

Fig 2 *Macroscopic appearance of the left lung after pneumonectomy.*

and on culture. At review one year after operation she was still well. Her ESR had fallen to 29 mm in one hour, she had gained a further 2 kg in weight, and laryngeal swabs were again negative for acid fast bacilli.

At pathological examination the excised left lung was so contracted and fibrotic that it was almost unrecognisable as lung tissue (fig 2). There were many fibrous adhesions on the pleural surface and a large ragged cavity 8 cm in diameter replaced most of the upper lobe. The lower lobe showed extensive bronchiectasis and fibrosis. Microscopically the appearances were characteristic of a mycobacterial infection with large areas of lung tissue replaced by multiple giant cell granulomas, many of which showed central necrosis. The large cavity was lined by granulation tissue, which in some areas contained giant cell granulomas. The bronchiectatic cavities were lined with a mixture of granulation tissue, columnar epithelium, and squamous epithelium. Ziehl-Nielson stains showed occasional acid fast bacilli, mainly within the necrotic lining of the large cavity. The lung tissue was cultured and grew *M malmoense.*

Discussion

M malmoense must be pathogenic as three of the 11 infections previously reported[2] were fatal. Unfortunately, as no clinical details are available the effect of drug treatment is unknown. None of the patients would appear to have had surgery.

A review of the diseases associated with atypical mycobacteria[4] states that underlying lung disease such as bronchiectasis and pneumoconiosis is common. *M malmoense* is not mentioned in this article,[4] but our case and those reported by Jenkins[2] (seven out of 11 had pneumoconiosis) would support that claim.

The in vitro drug resistance of *M malmoense* is similar to that found with the *Mycobacterium avium-intracellulare* group. The latter, however, tend to be resistant to antibiotics other than ethionamide and cycloserine.[3] Because the clinical significance of such in vitro drug resistance is unknown, the most effective drug regimen is problematical. We have no information about the efficacy of the drugs that are resistant in vitro in any other case of *M malmoense.* Our patient, who was compliant, failed to respond to nine months of drugs shown to be ineffective in vitro. In 64 patients with *Mycobacterium avium-intracellulare* infection reviewed[3] there was an 84% response (that is, clinical and radiographic improvement) to rifampicin, isoniazid, and either streptomycin or ethambutol, despite apparent drug resistance in vitro. There is no ready explanation for the apparent efficacy of this regimen, but it has been suggested that either the drugs are effective in vivo when the bacterial load is low or that there is a synergistic effect that has yet to be demonstrated in vitro (PA Jenkins, personal communication).

The rationale for adopting the same regimen for an infection with *M malmoense* lies in the close taxonomic relationship that exists between this species and the *M avium-intracellulare* complex. The species was originally described although not named in 1967, when five strains related to *M avium* were assigned to a "provisional species 2".[5] Its relationship was again emphasised in 1969[6] and in the description of the species in 1977 by Schroder and Juhlin,[1] who differentiated it from *M avium* and *M intracellulare* by a relatively small number of tests. It is too early to claim a cure in this patient, who has so far received one year of standard antituberculous chemotherapy since pneumonectomy. Hunter *et al*[3] recommend that 24 months of this regimen should be given.

It is certain that without surgery this patient would have died. It may be that the standard antituberculous drugs will now be effective as the bacterial load has been removed by operation.

We wish to thank Dr PA Jenkins for his most helpful advice.

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